REMARKS

Claims 49, 54, 56-58, 63, 66, 72, 75, 79 and 80 are pending and stand rejected. Applicants respectfully request reconsideration in view of the following remarks.

Rejection Under 35 U.S.C. § 101 and Rejection Under 35 U.S.C. § 112, First Paragraph

Claims 49, 54, 56-58, 63, 66, 72, 75, 79 and 80 are rejected under 35 U.S.C. § 101 and § 112, first paragraph, because the claimed invention allegedly is not supported by either a specific, substantial, and credible asserted utility or a well established utility. Applicants traverse this rejection and assert that the claimed genes (254P1D6B) and their encoded proteins are useful in diagnostic methods for detecting cancers that overexpress 254P1D6B, including, e.g., prostate. lung and ovarian cancers, and in methods of generating an immune response in a mammalian subject.

At the outset, Applicants note that the Examiner appears to confound the claimed gene, 254P1D6B, with the 284 polynucleotide SSH (suppression subtractive hybridization) sequence having SEQ ID NO:1 described in Figure 1. As the Examiner notes, the specification states that "the SSH DNA sequence (Figure 1) was designated 254P1D6B." *See* specification at, e.g., page 82, Example 2. Applicants call to the Examiner's attention that the specification also states that "the nucleotide (Figure 2) and amino acid (Figure 2, and Figure 3) sequences *of 254P1D6B* are provided." *See* specification at, e.g., page 4. Moreover, the specification states that "254P1D6B proteins are collectively referred to as the 254P1D6B-related proteins, the proteins of the invention or *254P1D6B*." *See* specification at, e.g, page 18. Accordingly, applicants respectfully submit that a person of skill in the art, reading the specification as a whole and in context, would understand that the term "254P1D6B" as used throughout the specification refers not only to the SSH sequence having SEQ ID NO:1, but more generally to the claimed gene, its encoded proteins, and/or variants thereof.

The Examiner insists that Applicants have not provided any objective evidence that the variant sequences can be used as cancer markers, because the specification allegedly fails to provide a nexus between expression of the 254P1D6B SSH sequence (SEQ ID NO:1) in cancerous tissues

and the expression of the individual sequence variants. The Examiner asserts that there are no teachings for how to use a polypeptide of claims 54 and 56 if said peptides do not generate an antibody which binds a polypeptide associated with a cancerous state. In addition, the Office cites Matsushita et al. (*FEBS Letters*, 1999, 443:348-352), Singh et al. (*Glycobiology*, 2001, 11:587-92), and Zwhalen et al. (*Int. J. Cancer*, 2000, 88:66-70) for the proposition that protein variants having different expression and function are known, and therefore asserts that a person of skill in the art cannot anticipate the biological activity or tissue distribution of a protein variant based on the wild type protein or a single protein isoform. The Office further asserts that claims 63, 66 and 72 (drawn to polynucleotides), and claim 58 (drawn to a method of generating an immune response) lack utility for the reasons set forth above with respect to the proteins. Thus, the Office concludes the utility requirement has not been satisfied. Applicants respectfully disagree, for at least the following reasons.

The Claimed Invention Has a Specific and Substantial Utility

The claimed polynucleotides have specific utility as diagnostic and prognostic markers for cancers that express 254P1D6B, including for example, prostate, lung and ovarian cancers. Under 35 U.S.C. § 101, a patent may be granted to "whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter." An invention may be useful for "any particular practical purpose (i.e., it has a "specific and substantial utility)." MPEP § 2107.

The Federal Circuit addressed the utility requirement in *In re Fisher*, 421 F.3d 1365, 76 USPQ.2d 1225 (Fed. Cir. 2005). The Court defined specific utility as "particular to the subject matter claimed" and "not applicable to a broad class of invention." *Id.* at 1372 (citing MPEP § 2107.01). For example, a specific utility could exist "where an applicant discloses a specific biological activity and reasonably correlates that activity to a disease condition." MPEP § 2107.01. In addition to being specific, an invention's utility must be substantial, where "a substantial utility defines a 'real world' use." *In re Fisher*, 421 F.3d at 1372. "*Any reasonable use* that an applicant has identified . . . that can be viewed as providing a public benefit should be accepted as sufficient,

at least with regard to defining a 'substantial' utility." MPEP § 2107.01 (emphasis added); *see also Nelson v. Bowler*, 626 F.2d 853, 856 (CCPA 1980).

An invention's "specific benefit" must also be in "currently available form." *Brenner v. Manson*, 148 U.S.P.Q. 689 (1966). In *Brenner*, the invention was a process for producing a novel hormone where the hormone's only utility was its potential role as an object of use-testing. The court held that the process was patentable only if the hormone itself had a specific and currently available benefit. However, this does not "mean that products or services based on the claimed invention must be 'currently available' to the public in order to satisfy the utility requirement." MPEP § 2107.01.

The applicant benefits from a presumption that his assertion of utility is correct. In *In re Brana*, 51 F.3d 1560, 1562 (Fed. Cir. 1995), the applicants claimed compounds for use as antitumor substances. The Federal Circuit reversed the Board's affirmation of the examiner's rejection, finding that the PTO did not meet its "initial burden of challenging a presumptively correct assertion of utility in the disclosure," and that "[t]he purpose of treating cancer with chemical compounds does not suggest an inherently unbelievable undertaking or involve implausible scientific principles." *Id.* at 1566.

Here, the applicants have asserted a specific, substantial utility—namely, that of indicating the presence of cancer. The specification teaches that the expression profile of 254P1D6B is related to cancer (Table 1), and that alternative transcripts and splice variants of 254P1D6B are also involved in cancers in the same or different tissues, thus serving as a family of tumor-associated markers/antigens. *See* specification at, e.g., page 83.

With respect to the assertion that specification fails to provide a nexus between the expression of the 254P1D6B SSH sequence (SEQ ID NO:1) in cancerous tissues and the expression of the individual variant sequences, applicants call to the Examiner's attention that the full length sequences of 254P1D6B, including inter alia, SEQ ID NOs:2, 4, and 6, were identified using the SSH sequence in a subtraction consisting of a prostate cancer xenograft LAPC-9AD^2 minus prostate

cancer xenograft LAPC-9AD. *See* specification at, e.g., pages 82, Example 2. Applicants note that nucleic acids 2776-2493 of SEQ ID NO: 2 represent the complement sequence of SEQ ID NO:1, differing by only one of 284 base pairs. Similarly, nucleic acids 2776-2493 of SEQ ID NO: 4, and nucleic acids 2976-2693 of SEQ ID NO: 6 represent complement sequences of SEQ ID NO:1. BLAST sequence alignments of SEQ ID NO:1 versus SEQ ID NO:2 (Exhibit 1), SEQ ID NO:4 (Exhibit 2), and SEQ ID NO:6 (Exhibit 3) are attached, showing 99% identity between SEQ ID NO:1 and the complementary sequences noted above. Accordingly, a probe capable of identifying SEQ ID NO:1 would reasonably be expected to identify polynucleotides having SEQ ID NOs:2, 4, and 6.

The Examiner asserts that in order to be used as a disease marker, one needs to know that a claimed polynucleotide is present only in cancerous tissue to the exclusion of normal tissue, or is expressed in higher levels in diseased versus normal tissue. (*See* Office action at page 4). The Examiner acknowledges that evidence of differential expression might serve as the basis for use of the claimed polynucleotide as a diagnostic for disease. Applicants call to the Examiner's attention the data presented in Figures 14-16, showing strong expression of 254P1D6B in lung and ovarian cancer pools, and in lung cancer patient specimens, but not in normal lung or in most normal tissues.

Based on the Northern blot data provided for 254P1D6B, the complementarity of SEQ ID NO:1 and the claimed polynucleotides sequences, and the derivation of the full length sequences encoding 254P1D6B using SSH from a prostate cancer xenograft, Applicants respectfully submit that a person of ordinary skill in the art would recognize that the claimed sequences are useful as diagnostic markers for cancer. Support for this specifically asserted utility is found, for example, in Example 4 and Figures 14-16 of the specification as originally filed. This utility is specific to the polypeptides claimed and not applicable to a broad range of inventions, which may or may not be expressed in cancerous cells. Moreover, like the example given in the MPEP, the claimed polypeptides have been correlated to a specific disease condition—prostate cancer.

The asserted utility is also substantial in that it provides a "real world use" for the claimed subject matter as a means for diagnosing prostate cancer. This use provides a genuine public benefit. The Examiner is reminded that the present lack of an immediately available commercial diagnosis for cancer based on the claimed polypeptide does not render the invention useless under *Brenner v. Manson*, 148 U.S.P.Q. 689 (1966). In *Brenner*, the invention was a process for producing a novel hormone where the hormone's only utility was its potential role as an object of use-testing. The court held that the process was patentable only if the hormone itself had a specific and currently available benefit. However, this does not "mean that products or services based on the claimed invention must be 'currently available' to the public in order to satisfy the utility requirement." MPEP § 2107.01.

Finally, Applicants' asserted utility carries the presumption of correctness and the Examiner failed to meet his initial burden in challenging the utility of the claimed protein. The purpose of detecting various cancers with antibodies using markers such as the claimed protein is neither inherently unbelievable nor implausible and the Examiner has not raised sufficient evidence to demonstrate otherwise.

Applicants have Provided Sufficient Evidence to Support the Asserted Utility

In a recent non-precedential decision, *Ex parte Goddard,* the Board held that microarray data demonstrating mRNA overexpression in cancerous tissues compared to non-cancerous tissues was sufficient to establish a specific and substantial utility for the claimed polynucleotide as a cancer marker. *See Ex parte Goddard*, Appeal 2006-1469 (BPAI 2007). As described above, the applicants have provided a nexus between the 254P1D6B SSH sequence (SEQ ID NO:1) and the expression of the individual variant sequences, including *inter alia* SEQ ID NOs:2, 4, and 6, by identification of the variant sequences in a prostate cancer xenograft. Applicants respectfully direct the Examiner to the data provided in Example 4, and Figures 14-16, which demonstrate that mRNA corresponding to the claimed 254P1D6B proteins is over-expressed in various cancer cell lines and cancerous tissues relative to normal tissues. Accordingly, applicants respectfully submit that the

data provided is sufficient to allow one of ordinary skill in the art to reasonably conclude that the claimed 254P1D6B proteins are useful to detect, e.g., prostate, lung, and ovarian cancers.

The Office has not stated a prima facie *case*

The Office has not made a *prima facie* showing that one of ordinary skill in the art would reasonably doubt that the claimed proteins are useful as diagnostic targets. When making a rejection for an alleged lack of utility, the Office must make a *prima facie* showing that the claimed invention lacks utility and it must provide sufficient evidence to support the basis of that *prima facie* showing. *In re Gaubert*, 524 F.2d 1222, 1224 (CCPA 1975); MPEP § 2107.2. In contrast, Applicants need only disclose a single specific and substantial utility to satisfy the requirement of the statute. *In re Fisher*, 421 F.3d 1365, 1370 (Fed. Cir. 2005).

Applicants have provided evidence that the claimed sequences are present in prostate cancer xenografts, and further showing that mRNA encoding the claimed proteins is detected in certain cancer cells. Nothing more need be shown to satisfy the utility requirement. Accordingly, Applicants respectfully request that the present rejection of the claims under 35 U.S.C. § 101 and 35 U.S.C. § 112, first paragraph, be withdrawn and the present application be passed to issuance.

CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 511582008100. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Dated: November 13, 2007

Respectfully submitted,

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NCBI Blast 2 Sequences results

BLAST 2 SEQUENCES RESULTS VERSION BLASTN 2.2.17 [Aug-26-2007]

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Masking character option X for protein, n for nucleotide Masking color option Black
☐ Show CDS translation Align

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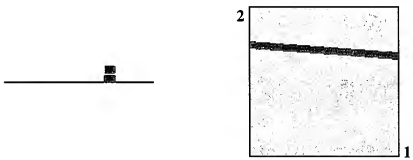

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NOTE:If protein translation is reversed, please repeat the search with reverse strand of the query sequence.

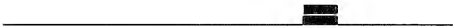

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EXHIBIT 1

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NCBI **Blast 2 Sequences results**

PubMed Entrez BLAST OMIM Taxonomy Structure

BLAST 2 SEQUENCES RESULTS VERSION BLASTN 2.2.17 [Aug-26-2007]

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Masking character option X for protein, n for nucleotide Masking color option Black
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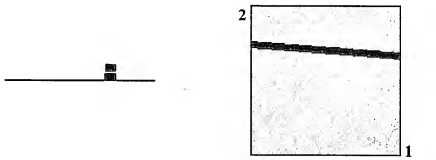

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NOTE:If protein translation is reversed, please repeat the search with reverse strand of the query sequence.

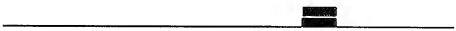

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EXHIBIT 2

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Blast 2 Sequences results

PubMed Entrez BLAST OMIM Taxonomy Structure

BLAST 2 SEQUENCES RESULTS VERSION BLASTN 2.2.17 [Aug-26-2007]

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Masking character option X for protein, n for nucleotide Masking color option Black
Show CDS translation Align

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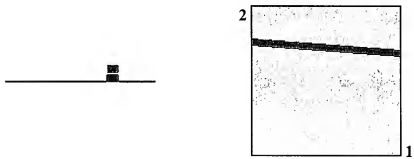

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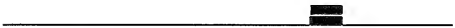

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EXHIBIT 3

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